

## **REMARKS**

### **Status of the Claims**

Claims 19-21 have been cancelled.

Claim 18 has been amended. Support for this amendment can be found in the Specification at, for example, page 5, lines 12-13 and page 6, lines 9-16.

Claims 36-38 have been added. Support for the new claims can be found in the Specification, namely at page 8, lines 1-3.

### **Claim Rejections – 35 U.S.C. § 103**

The only rejection of the claims is that of claims 18-27 and 30-35 under 35 U.S.C. § 103(a) over *Willoughby et al.* (WO 94/23725) in view of *Pressato et al.* (WO 97/07833). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner will first of all note that claim 18 is now limited to a method of using the total benzyl ester to inhibit angiogenic processes related to vascularisation “by granulation tissue forming over the biomaterial”.

The essence of the Examiner’s rejection is best set forth in the second full paragraph on page 6 of the Office Action wherein the Examiner states that “one having ordinary skill in the art would have been motivated in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) consisting essentially of a benzyl ester of hyaluronic acid, since Willoughby suggests the esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes,

woven tissues or meshes and non-woven tissues (of a biomaterial) that can be administered directly to a treated site.”

Applicant submits that the Examiner’s position fails to properly consider the teachings of the prior art references as a whole, and improperly remains fixed on an allegation of *prima facie* obviousness in spite of the evidence; rather simply based on an improper hindsight view of the prior art.

First of all, the Examiner improperly interprets *Willoughby et al.* to suggest that “hyaluronic acid is therapeutically effective substance or component for inhibiting or treating angiogenesis” (see page 9, lines 2-4 of the Office Action). *Willoughby et al.* actually only teaches that a combination of hyaluronic acid with a NSAID can be effective for controlling and/or regressing angiogenesis. In the Office Action, the Examiner points to the abstract of *Willoughby et al.* However, the abstract clearly teaches the use of a combination of “(a) a non-steroidal anti-inflammatory agent, and (b) hyaluronic acid..., wherein dosage amounts taken from the composition each comprise: (1) a therapeutically effective amount of component (a) and (2) a therapeutically effective amount of the hyaluronic acid...”. All of the remaining disclosures in *Willoughby et al.* similarly are focused on the use of a combination of a NSAID and hyaluronic acid (see, for example, page 7, lines 17-22; page 8, lines 20-27; page 8, lines 29-32; page 8, lines 34-36; page 9, lines 25-32; page 10, lines 6-11; page 10, lines 25-34 and page 11, lines 1-12). Indeed, the paragraph bridging pages 10 and 11 of the Specification specifically teaches that the composition containing the form of hyaluronic acid and NSAID provides greater inhibition and regression of angiogenesis than a composition comprising a form of hyaluronic acid only (i.e. without a NSAID). There is simply no teaching in *Willoughby et al.* to suggest the use of hyaluronic acid alone for inhibiting, controlling and/or regressing angiogenesis. As such, the fundamental basis for the Examiner’s rejection is mistaken, so that the entire *prima facie* obviousness position of the Examiner is improper.

Since *Willoughby et al.* only teaches that a combination of hyaluronic acid with a NSAID can be used to inhibit angiogenesis, one skilled in the art would not be led to use any derivative or ester of hyaluronic acid to inhibit angiogenesis.

The Examiner will also note that claim 18 has been amended to recite that the biomaterial that inhibits angiogenic processes related to vascularisation “by granulation tissue forming over the biomaterial”. This is contrary to *Willoughby et al.* wherein the experimentally induced granulation tissue is actually reduced as a consequence of the effects of the treatment. *Willoughby et al.*, therefore, in this respect is again opposite to the presently claimed method. Applicant submits that the Examiner is simply taking a hindsight view of the prior art with the advantage of the Applicant’s present application, without properly viewing the teachings of the prior art as a whole and viewing the teachings of the prior art as one of skill in the art viewing the prior art without Applicant’s present application. The Examiner emphasizes several times that the present rejection is based on a combination of *Willoughby et al.* and *Pressato et al.*, not based on a combination of *Willoughby et al.* with some other publications noted by Applicant, such as *Willhauck et al.* While Applicant recognizes that the Examiner’s rejection is not based on a combination of *Willoughby et al.* with these other publications, the Examiner’s critique misses the point. Applicant’s point is that the Examiner’s selection of *Pressato et al.* as a secondary reference is based only on the Examiner’s desire to find some prior art reference that teaches benzyl esters of hyaluronic acid *per se*, and not based on the view of one skilled in the art at the time of Applicant’s invention.

*Pressato et al.* teaches nothing concerning inhibition of angiogenesis or of tumor growth, nor anything regarding granulation tissue. As such, the proper frame of reference for the Examiner is to consider what one skilled in the art would be led to when viewing the prior art at the time of Applicant’s invention. In addition to the publications referenced in Applicant’s prior response, one skilled in the art would know of the teaching of *Abatangelo et al.*, WO 98/56897 (enclosed as Exhibit A), which teaches the use of a non-woven material based on the total benzyl ester Hyaff®11 to induce the growth of endothelial cells. Figure 1 of this publication discloses the

growth of these cells (HUVEC) by non-woven support material based on the total benzyl ester product Hyaff®11. Figure 2 of the publication discloses the same experiment using collagen a support. In comparison of the results of the two experiments shows that the endothelial cells grow much better on the Hyaff®11 based material (see also pages 7-8 of *Abatangelo et al.*). Thus, one skilled in the art confronted with the teachings of *Willoughby et al.* and even motivated to find a substitute for hyaluronic acid as taught by *Willoughby et al.*, would look for references and would find both *Pressato et al.* and *Abatangelo et al.* Such a person would have no reason to select *Pressato et al.* as teaching an alternative hyaluronic acid benzyl ester to inhibit angiogenesis because *Abatangelo et al.* teaches the opposite of what is disclosed in the present application. In other words, one skilled in the art would not ignore prior art teachings in the direction opposite of the present invention, and thus would not be led to combine the teachings of *Willoughby et al.* with those of *Pressato et al.* in the manner suggested by the Examiner.

In view of the above, Applicant submits that the Examiner's *prime facie* case of obviousness is improper and should be withdrawn.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of \$1,110.00 is attached hereto.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Application No. 10/501,030  
Amendment dated July 8, 2009  
After Final Office Action of January 8, 2009

Docket No.: 0471-0286PUS1

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: July 8, 2009

Respectfully submitted,

By 

Leonard R. Svensson

Registration No.: 30,330

BIRCH, STEWART, KOLASCH & BIRCH, LLP

12770 High Bluff Drive

Suite 260

San Diego, California 92130

(858) 792-8855

Attorney for Applicant